

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-27. (canceled)

28. (currently amended) A method for testing and selecting an agent ~~to determine whether said agent inhibits or stimulates~~ that has an activity on clonal growth, comprising the steps:

a) testing said agent having an activity on clonal growth with an *in vitro* clonal test to study the effect of said agent on cloning, the *in vitro* clonal step a) comprising:

i) seeding solitary [[of]] cells in a ~~suitable~~ soft agar medium with or without growth factor,

ii) incubating said cells in a low gelling temperature gel at a suitable temperature and atmosphere with said agent having an activity on clonal growth; and

iii) determining the effect of said agent having an activity on clonal growth on cloning of said cells;

b) testing the effect that different degrees of local collocation of cells has on the effect of said agent having an activity on clonal growth on cloning, the testing the effect step b) comprising:

i) transplanting [[a]] tumor ~~cell~~ cells to an animal, or seeding experimental cell cultures with any of ~~the mentioned~~ said cells;

ii) treating the animal with said tumor ~~cell~~ cells or the cells in experimental cell cultures with said agent;

iii) determining the effect of said agent having an activity on clonal growth on cloning of said tumor ~~cell~~ cells in the animal or of the cells in experimental cell cultures;

c) testing said agent having an activity on clonal growth with an *in vivo* metastasizing test that determines the effect of said agent having an activity on clonal growth on metastasizing cells, the testing said agent step c) comprising:

i) injecting tumor cells in an animal to develop metastases, ascites or local tumors;

ii) applying the agent having an activity on clonal growth; and

iii) determining the effect of said agent having an activity on clonal growth to affect the liberation of cells, migration, and the ability to form a local tumor;

d) testing said agent having an activity on clonal growth with an *in vivo* test of clonal growth of immune cells stimulated by immunization;

e) evaluating the results obtained with steps a), b), c) and d); and

f) determining and selecting said agent having an activity on clonal growth.

29. (canceled)

30. (previously presented) The method according to claim 28, wherein the clonal test is performed in:

- i) a fluid medium; or
- ii) a semisolid or solid medium

31. (previously presented) The method according to claim 28, wherein the cells are malignant cells, normal cells, cell lines, transformed cells and cells from a tumor or malignant disease of a patient.

32. (currently amended) The method according to claim [[u]]28, wherein the cells are immune cells that are cloned and selected after immunization.

33. (previously presented) The method according to claim 28, wherein the cells are selected from the group consisting of BHK21/c13, and BHK21/C13 cells transformed with polyoma virus.

34. (previously presented) The method according to claim 28, wherein the medium further comprises insulin, serum, insulin like growth factors, cytokines, or serum extenders, and conditioned medium or a combination of these.

35-36. (canceled)

37. (previously presented) The method according to claim 28, wherein said tumor cells are transplanted Ehrlich carcinoma cells.

38. (previously presented) The method according to claim 28, wherein said method detects an agent that causes an increased number of clones and/or facilitates the growth and migration of metastases and/or growth of primary tumors.

39. (canceled)

40. (currently amended) The method according to claim 28, wherein the agent is selected from the group consisting of drugs, food, food additives, toxins, ~~potential toxins~~, microbes, a component of a physiological or a pathological process.

41. (previously presented) The method according to claim 28, wherein the agent is a drug.

42. (previously presented) The method according to claim 28, wherein the agent is a food.

43. (previously presented) The method according to claim 28, wherein the agent is a food additive.

44. (previously presented) The method according to claim 28, wherein the agent is a toxin.

45. (currently amended) The method according to claim 28, wherein the agent is a ~~mireobe~~ microbe.

46. (previously presented) The method according to claim 28, wherein the agent is a component of a physiological or a pathological process.

47. (previously presented) A method for inhibiting clonal cell growth, comprising, administering to cells an effective amount of a clonal mitotic inhibitor determined by the method according to claim 28.

48. (currently amended) The method according to claim 47, wherein the clonal mitotic inhibitors are selected from the group consisting of 4-OH-OPB, ~~Kolchicin~~ colchicine, Ibuprofen, Naproxen, ~~Acetyl~~ acetyl salicylic acid, ~~p-hydroxy azobenzene, 2-~~

~~Butyl-2-hydroxy-N-(4-hydroxy-phenyl)-N'-phenyl malonamide, 1,2-diphenyl-4-hydroxy-4-[2-(phenylsulfinyl)ethyl]-3,5-pyrazolidinedione, and analogues thereof.~~

49. (previously presented) The method according to claim 48, wherein the cells are tumor cells.

50. (previously presented) A method for inhibiting clonal cell growth in a subject, comprising: administering to subject an effective amount of a clonal mitotic inhibitor determined by the method according to claim 28.

51. (currently amended) The method according to claim 50, wherein the clonal mitotic inhibitors are selected from the group consisting of 4-OH-OPB, ~~Kelchicin~~ colchicine, Ibuprofen, Naproxen, ~~Acetyl~~ acetyl salicylic acid, p-hydroxy-azobenzene, 2-Butyl-2-hydroxy-N-(4-hydroxy-phenyl)-N'-phenyl malonamide, 1,2-diphenyl-4-hydroxy-4-[2-(phenylsulfinyl)ethyl]-3,5-pyrazolidinedione, and analogues thereof.

52. (currently amended) The method according to claim 51, wherein the ~~patient~~ subject has or is at risk of developing a disorder selected from the group consisting of arteriosclerosis, an autoimmune disorder, a rejection of a transplant, and a

disorder related to cell growth initiated by radioactivity, and viral growth in cells of the organism.

53. (previously presented) The method according to claim 52, wherein said viral growth is due to HIV or Herpes infection.

54. (currently amended) The method according to claim 53, wherein 4-OH-OPB is administered to a subject after said subject has been exposed or infected to HIV and before HIV infected cells ~~are piling up~~ proliferate.

55. (currently amended) The method according to claim 53, wherein 4-OH-OPB is administered to a subject with chronic infections or AIDS after removing [[the]] collocated infected cells.

56. (previously presented) The method according to claim 53, wherein 4-OH-OPB is administered in combination with an anti-viral treatment to inhibit drug resistance.

57. (previously presented) The method according to claim 52, wherein 4-OH-OPB is administered as an initial treatment to a subject in order to inhibit metastasis of a cancer.

58. (previously presented) The method according to claim 52, wherein 4-OH-OPB is administered to a subject undergoing conventional cancer treatment.

59. (previously presented) A method for stimulating clonal cell growth, comprising: administering to cells an effective amount of a clonal mitotic stimulator determined by the method according to claim 28.

60. (currently amended) The method according to claim 59, wherein the clonal mitotic stimulators comprise insulin, insulin like growth factors, conditioned medium, serum factors, Mito+, or serum extenders, ~~Diclofenak, Sulindak~~ or Benzo(a)pyrene and analogues thereof.

61. (currently amended) A method for testing an agent ~~to determine whether said agent inhibits or stimulates~~ that has an activity on clonal growth, comprising the steps:

a) testing said agent having an activity on clonal growth with an *in vitro* clonal test for studying the effect of said agent on cloning, said cloning test comprising:

- i) seeding of solitary cells in a soft agar medium with or without growth factor,
- ii) incubating said cells in a low gelling temperature gel at a suitable temperature and atmosphere with



said agent having an activity on clonal growth;  
and

iii) determining the effect of said agent having an activity on clonal growth on cloning of said cells;

b) testing the effect that different degrees of local collocation of cells have on the effect of said agent having an activity on clonal growth on cloning, said testing comprising:

i) transplanting [[a]] tumor ~~cell~~ cells to an animal, or seeding experimental cell cultures with BHK21/c13 or BHK21/C13 cells transformed with polyoma virus;

ii) treating said tumor ~~cell~~ cells in the animal or the cells in experimental cell cultures with said agent having an activity on clonal growth;

iii) determining the effect of said agent having an activity on clonal growth on cloning of said tumor ~~cell~~ cells or stimulated immune cells in the individual or the cells in experimental cell cultures;

c) testing said agent having an activity on clonal growth with an *in vivo* metastasizing test to determine the effect of said agent having an activity on clonal growth on metastasizing cells, said step comprising:

- i) injecting tumor cells in an animal to develop metastases, ascites or local tumors;
  - ii) applying the agent having an activity on clonal growth; and
  - iii) determining the effect of said agent having an activity on clonal growth to affect the liberation of cells, migration, and the ability to form local tumor;
- d) evaluating the results obtained with steps a), b), and c); and
- e) determining whether said agent having an activity on clonal growth inhibits or stimulates clonal growth.

62. (new) A method for testing and selecting a food, a food additive or a microbe that has an activity on clonal growth, comprising the steps:

a) testing said food, food additive or microbe having an activity on clonal growth with an *in vitro* clonal test to study the effect of said food, food additive or microbe on cloning, the *in vitro* clonal step a) comprising:

- i) seeding cells in a suitable medium with or without growth factor,
- ii) incubating said cells in at a suitable temperature and atmosphere with said food, food additive or microbe having an activity on clonal growth; and

iii) determining the effect of said food, food additive or microbe having an activity on clonal growth on cloning of said cells;

b) testing the effect that different degrees of local collocation of cells has on the effect of said food, food additive or microbe having an activity on clonal growth on cloning, the testing the effect step b) comprising:

i) transplanting tumor cells to an animal, or seeding experimental cell cultures with any of the cells;

ii) treating the animal with said tumor cells or the cells in experimental cell cultures with said food, food additive or microbe;

iii) determining the effect of said food, food additive or microbe having an activity on clonal growth on cloning of said tumor cells in the animal or of the cells in the experimental cell cultures;

c) testing said food, food additive or microbe having an activity on clonal growth with an *in vivo* metastasizing test that determines the effect of said agent having an activity on clonal growth on metastasizing cells, the testing said food, food additive or microbe step c) comprising:

i) injecting tumor cells in an animal to develop metastases, ascites or local tumors;

ii) applying the food, food additive or microbe having an activity on clonal growth; and

iii) determining the effect of said food, food additive or microbe having an activity on clonal growth to affect the liberation of cells, migration, and the ability to form a local tumor;

d) testing said food, food additive or microbe having an activity on clonal growth with an *in vivo* test of clonal growth of immune cells stimulated by immunization;

e) evaluating the results obtained with steps a), b), c) and d); and

f) determining and selecting said food, food additive or microbe having an activity on clonal growth.

63. (new) A method for testing and selecting an agent that has an activity on clonal growth, the agent being selected from drugs, potential drugs, food, food additives, toxins, potential toxins, components from physiological or pathological processes including microbes or components of a physiological or pathological process, comprising the steps:

a) testing said agents having an activity on clonal growth, with an *in vitro* clonal test to study the effect of said agents on cloning, the *in vitro* clonal step a) comprising:

i) seeding solitary cells in a suitable soft agar medium with or without growth factor,

ii) incubating said cells in a low gelling temperature gel at a suitable temperature and atmosphere with said agent having an activity on clonal growth; and

iii) determining the effect of said agent having an activity on clonal growth on cloning of said cells;

b1) testing said agents, having an activity on clonal growth, to study the effect of said agents on different degrees of local collocation of cells seeded sparsely in agar culture or transplanted as single cells sufficiently diluted and scattered in tissues, comprising:

i) transplanting tumour cells to an animal, or seeding experimental cell cultures with any of said cells;

ii) treating the animal with said tumor cells or the cells in experimental cell cultures with said agent;

iii) determining the effect of said agent on cloning of said tumor cells in the animal or of the cells in experimental cell cultures;

c) testing said agent with an *in vivo* metastasizing test that determines the effect of said agent on metastasizing cells, the testing said agent step c) comprising:

i) injecting tumor cells in an animal to develop metastases, ascites or local tumors;

ii) applying the agent; and

iii) determining the effect of said agent to affect the liberation of cells, migration, and the ability to form a local tumor;

d) testing said agent with an *in vivo* test of clonal growth of immune cells stimulated by immunization;

e) evaluating the results obtained with steps a), b), c) and d); and

f) determining and selecting said agent.